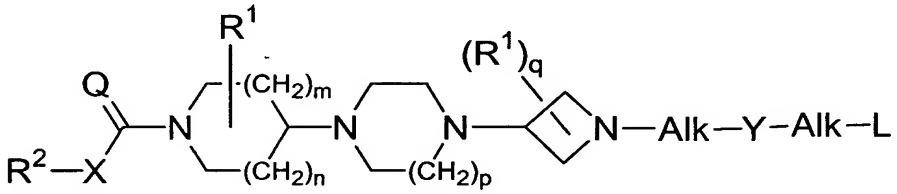
ABSTRACT

SUBSTITUTED 1-PIPERIDIN-4-YL-4-AZETIDIN-3-YL-PIPERAZINE DERIVATIVES AND THEIR USE AS NEUROKININ ANTAGONISTS

The invention concerns substituted 1-piperidin-4-yl-4-azetidin-3-yl-piperazine having neurokinin antagonistic activity, in particular NK_1 and NK_1/NK_3- antagonistic activity, their preparation, compositions comprising them and their use as a medicine, in particular for the treatment of schizophrenia, emesis, anxiety, depression, irritable bowel syndrome (IBS), circadian rhythm disturbances, pain, neurogenic inflammation, asthma, micturition disorders such as urinary incontinence and nociception. The compounds according to the invention can be represented by general Formula (I)



(I)

and comprises also the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1.

In view of their capability to antagonize the actions of tachykinins by blocking the neurokinin receptors, and in particular antagonizing the actions of substance P by blocking the NK receptors, the compounds according to the invention are useful as a medicine, in particular in the prophylactic and therapeutic treatment of tachykinin-mediated conditions, such as, for instance CNS disorders, in particular depression, anxiety disorders, stress-related disorders, sleep disorders, cognitive disorders, personality disorders, schizoaffective disorders, eating disorders, neurodegenerative diseases, addiction disorders, mood disorders, sexual dysfunction, pain and other CNS-related conditions ; inflammation ; allergic disorders ; emesis ; gastrointestinal disorders, in particular irritable bowel syndrome (IBS); skin disorders ; vasospastic diseases ; fibrosing and collagen diseases ; disorders related to immune enhancement or suppression and rheumatic diseases and body weight control.